IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Sudhir Agrawal, Lakshmi Bhagat, Dong Yu and Ekambar R. Kandimalla		
Application No.:	10/757,345	Group:	1633
Filed:	January 14, 2004	Examiner:	Hill, Kevin Kai
Confirmation No.	3490		
For:	MODULATION OF IMMUNOSTIMULATORY PROPERTIES OF OLIGONUCLEOTIDE-BASED COMPOUNDS BY UTILIZING MODIFIED IMMUNOSTIMULATORY DINUCLEOTIDES		

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date indicated below.

Date: 10/1/08 Signature M Simpson

Printed Name: M SIMPSON

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DECLARATION PURSUANT TO 37 C.F.R. §1.132

Dear Sirs:

. I, Ekambar Kandimalla hereby declare as follows.

1. I am employed by Idera Pharmaceuticals, Inc. in the position of Senior Director of Research. A copy of my *Curriculum vitae* is attached as Exhibit 1.

2. I understand that Claims 1 and 31 are rejected as being obvious in view of Kandimalla (2001), Kandimalla (757) and Simmonds (1999). However, I do not believe that the instantly claimed genus of immunostimulatory oligonucleotides is obvious in view of the cited references.

3. It was previously known that oligonucleotides having a dinucleotide of the formula 5'-pyrimidine-purine-3', specifically a CG dinucleotide wherein the C is unmethylated, are capable of stimulating an immune response.

4. It was also previously demonstrated that modifications to this CG dinucleotide, for example methylating the C of the dinucleotide, reduced or abolished the immunostimulatory activity of the oligonucleotide.

5. I am an author of Kandimalla (2001). This reference described various modifications to the CG dinucleotide. Some of these modifications reduced or abolished the immunostimulatory activity of the oligonucleotide, while others increased the immunostimulatory activity. One modification referred to in the present rejection is the substitution of the unmethylated-C in the CG dinucleotide with the bicyclic cytosine analog deoxy-P-base. As stated in Kandimalla (2001), modifying the CG dinucleotide with deoxy-P-base resulted in an oligonucleotide that showed little or no immunostimulatory activity. As an author of this reference, I can attest that this meant that it was a non-functioning molecule and that the phrase "showed little or no immunostimulatory activity" meant that those modifications were inactive (i.e., not immunostimulatory). Therefore, contrary to the assertion in the Office Action, this oligonucleotide does not meet the functional limitations of the instantly claimed genus.

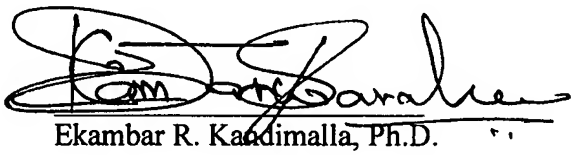
6. The Office Action states that deoxy-P-base and the instantly claimed modification are structurally similar and points to the teaching in Kandimalla ('757) which states that "cytosine has two hydrogen bond acceptor groups at positions 2 (keto-oxygen) and 3 (nitrogen), and a hydrogen bond donor group at the 4-position (amino group). These groups can serve as potential recognizing and interacting groups with receptors that are responsible for immune stimulation." However, the Office Action ignores two critical points with regards to this statement. It ignores that this statement teaches that these groups can serve as **potential** recognizing and interacting groups with receptors since the exact mechanism of receptor-ligand interaction is not known. It also ignores that despite any structural similarity between deoxy-P-base and the instantly claimed modification, a CG-containing oligonucleotide having a deoxy-P-base modification resulted in a non-functioning molecule whereas the instantly claimed modification resulted in a functional molecule.

7. The Office Action correctly points out that Kandimalla (2001) describes linear CG-containing oligonucleotides rather than an "immunomer" (i.e., two oligonucleotides linked at their 3'ends via a non-nucleotidic linker). However, the linking of two non-functioning

molecules (e.g., two CG-containing oligonucleotide having a deoxy-P-base modification) at their 3'ends via a non-nucleotidic linker would not result in a functioning molecule.

8. As such, I believe that instant claims 1 and 31 are not obvious in view of the art cited in the Office Action.

9. I hereby further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signed: 

Ekambar R. Kandimalla, Ph.D.

Dated: September 30, 2008